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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/099,663	03/14/2002	Nelson D. Horseman	AVI021	2987

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EXAMINER	
QIAN, CELINE X	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 01/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/099,663	HORSEMAN ET AL.	
	Examiner	Art Unit	
	Celine X Qian Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *50,53-56,58-61,66,69-75,77-81 and 87-107* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *50,53-56,58-61,66,69-75,77-81 and 87-107* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2002* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/18/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 50, 53-56, 58-61, 66, 69-75, 77-81, 87-107 are pending in the application.

Election/Restrictions

Applicant's election without traverse of Group I in the reply filed on 9/27/04 is acknowledged.

Claim Rejections - 35 USC § 101

Claims 77-80, 83, 102-105 and 107 are rejected under 35 U.S.C. 101 because they are not directed to statutory subject matter. The claims encompass human subjects. It is PTO policy not to issue claims that encompass humans (see 1077 OG 24, April 21, 1987).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50, 53-56, 58-61, 66, 69-75, 77-81, 87-107 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The written description requirement is set forth by 35 U.S.C. 112, first paragraph which states that the: "*specification* shall contain a written description of the invention. . .[emphasis added]." The written description requirement has been well established and characterized in the

case law. A specification must convey to one of skill in the art that "as of the filing date sought, [the inventor] was in possession of the invention." See *Vas Cath v. Mahurkar* 935 F.2d 1555, 1560 19 USPQ2d 1111, 1117 (Fed. Cir. 1991). Applicant may show that he is in "possession" of the invention claimed by describing the invention with all of its claimed limitations "by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention." See *Lockwood v. American Airlines Inc.* 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997).

In analyzing whether the written description requirement is met, it is first determined whether a representative number of species have been described by their complete structure. Next, it is determined whether a representative number of species have been sufficiently described by other relevant identifying characteristics. The claimed genus of isolated nucleic acid molecules (claims 50, 53-56, 58-61, 88-92) encompasses potentially a large number of nucleic acid sequences of various structure and size that have sequence homology with SEQ ID NO:1 (75-100%) and/or SEQ ID NO:2, wherein such nucleic acid molecule may not even be related to a gene expression controlling region. SEQ ID NO:1 is a 2.3 kb fragment 5' to chicken iFABP gene and SEQ ID NO:2 is a portion of SEQ ID NO:1. The specification discloses that two fragments from the chicken iFABP gene (0.6 and 1.6 kb) direct expression of the reporter gene in a rat duodenum and a mouse gut epithelial cell lines, whereas one 1.1 kb fragment fails to show promoter activity in the reporter gene assay. The specification fails to teach whether the nucleic acid fragment represented by SEQ ID NO:1 or SEQ ID NO:2 have promoter activity. The specification also fails to teach whether nucleic acid molecules having sequence homology (75-99%) with SEQ ID NO:1 and/or SEQ ID NO:2 possess promoter activity. Although SEQ ID

NO:2 comprises putative transcription factor binding sites common to iFABP from other species, the specification fails to disclose whether this 0.3 kb fragment is sufficient for promoter activity. Moreover, the specification only discloses that chicken iFABP 5' region that regulates gene transcription. It fails to disclose nucleic acid fragments that functions as other gene expression controlling region(s), for example, posttranscriptional regulatory region or trans-element for regulating gene expression. The specification also fails to disclose element(s)/structure(s)/sequence(s) the claimed fragments must share for said promoter or gene expression controlling function. As such, the structural and functional relationship between the claimed nucleic acid molecules and their promoter function is missing. Therefore, the written description requirement is not met.

Claims 66, 69-75, 77-81, 87, 93-107 recite gene controlling region comprising nucleotide sequences that hybridize under moderate stringency condition to SEQ ID NO:1 or SEQ ID NO:2. The claimed genus of nucleic acid molecules potentially encompasses a large number of polynucleotides or oligos of varying sizes and structure that may not even be a gene expression controlling sequence. As discussed above, the specification only discloses that two fragments from the chicken iFABP gene (0.6 and 1.6 kb) direct expression of the reporter gene in a rat duodenum and a mouse gut epithelial cell lines, whereas one 1.1 kb fragment fails to show promoter activity in the reporter gene assay. The specification fails to teach whether the nucleic acid fragment represented by SEQ ID NO:1 or SEQ ID NO:2 have promoter activity. The specification also fails to teach other nucleic acid fragments of SEQ ID NO:1 or SEQ ID NO:2 or oligonucleotides that hybridize to SEQ ID NO:1 or SEQ ID NO:2 have gene expression control activity. Furthermore, the specification fails to disclose

element(s)/structure(s)/sequence(s) the claimed fragments must share for said promoter or gene expression controlling function. As such, the structural and functional relationship between the claimed nucleic acid molecules and their promoter function is missing. Therefore, the written description requirement is not met.

Claims 77-80, 83, 102-105 and 107 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of expressing a polypeptide as claimed *in vitro*, and a *in vitro* cultured host cell comprising an expression vector which includes a gene expression controlling region operably linked to a nucleotide sequence encoding a polypeptide, does not reasonably provide enablement for such method when performed *in vivo* that encompasses transgenic animal, and a host cell that is *in vivo*. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/use the invention commensurate in scope with these claims.

The nature of the invention is a eukaryotic host cell comprising an expression vector comprising a gene controlling region and a gene encoding a polypeptide. The claims are further drawn to a method of expressing a polypeptide in a host cell by maintaining said host cell under conditions suitable for expression of the polypeptide.

The breadth of the claims is broad. The claims encompass human, transgenic animal and host cell comprising an expression vector comprises a gene controlling region operably linked to a nucleic acid sequence encoding a polypeptide.

The teaching of the specification is limited. The specification only enables the scope of an *in vitro* cultured host cell comprising an expression vector comprises a gene controlling

region operably linked to a nucleic acid sequence encoding a polypeptide, and method of making a polypeptide by using said host cell *in vitro*. The specification fails to teach any transgenic animal that comprising said expression vector in its genome. The specification further fails to teach a phenotype that is associated with transgenic animal comprising the expression. In addition, the specification fails to teach producing polypeptide using a transgenic animal having the expression vector.

The state of art at the time of filing teaches that making a transgenic animal with predicted phenotype as highly unpredictable. The phenotype of the transgenic animal is a required element for the enablement of the claimed invention because one would not know how to use the transgenic animal without any phenotype. Since the instant specification does not teach how to make a transgenic animal with predicted phenotype, nor does the specification provides any working example of a transgenic animal with a specific phenotype, one of skilled in the art would have to engage in undue experimentation to make and use the claimed invention. Therefore, the claims are not enabled to their full scope.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50, 53-56, 58-61, 66, 69-75, 77-81, 87-107 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claims 50, 53-56, 58-61, 66, 69-75, 77-81, 87-107, the recitation of "having at least ...identity to SEQ ID NO:1/SEQ ID NO:2 or its complement" or "hybridizes under

moderate stringent condition ...of SEQ ID NO:1/SEQ ID NO:2 or its complement" renders the claims indefinite because it appears redundant to recite the complement. In other words, the complementary sequence of SEQ ID NO:1/SEQ ID NO:2 has the same sequence as the one depicted as SEQ ID NO:1/SEQ ID NO:2, thus a nucleic acid sequence having homology with SEQ ID NO:1/SEQ ID NO:2 would have same homology with the complementary sequence. Similarly, a nucleic acid hybridizes to the sequence of SEQ ID NO:1/SEQ ID NO:2 would also hybridize to its complementary sequence.

Regarding claims 70 and 97, the word "derived" renders the claim indefinite because the nature and number of derivative process is unknown. As such, the metes and bounds of the claim cannot be established.

Regarding claims 87, 71, 94 and 95, the recitation of "a gene expression controlling region...further comprises a nucleotide sequence encoding a polypeptide" renders the claim indefinite because the gene expression controlling region is a region regulates the expression of a gene, not the gene itself. It is unclear whether the nucleotide sequence encoding the polypeptide is capable of having the regulatory function of gene expression, or it is the gene that is regulated by the controlling region. As such, the metes and bounds of the claim cannot be established.

Regarding claims 71, 83, 95 and 107, the recitation of "a codon complement optimized for protein expression..." renders the claim indefinite because it is unclear how the codon complements for protein expression.

Regarding claims 72-75, 98-101, the recitation of "a gene expression controlling region further comprising a vector" renders the claim indefinite because it is unclear whether the vector is part of the gene expression controlling region.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Celine X Qian Ph.D. whose telephone number is 571-272-0777. The examiner can normally be reached on 9:30-6:00 M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Celine X Qian Ph.D.
Examiner
Art Unit 1636

CELIAN QIAN
PATENT EXAMINER